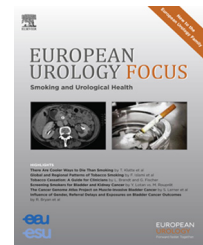


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Epidemiology

## Is There an Association Between Ambient Air Pollution and Bladder Cancer Incidence? Analysis of 15 European Cohorts

Marie Pedersen<sup>a,b,\*</sup>, Massimo Stafoggia<sup>c,d</sup>, Gudrun Weinmayr<sup>e</sup>, Zorana J. Andersen<sup>b</sup>,  
Claudia Galassi<sup>f</sup>, Johan Sommar<sup>g</sup>, Bertil Forsberg<sup>g</sup>, David Olsson<sup>g</sup>, Bente Oftedal<sup>h</sup>,  
Norun H. Krog<sup>h</sup>, Geir Aamodt<sup>i</sup>, Andrei Pyko<sup>d</sup>, Göran Pershagen<sup>d</sup>, Michal Korek<sup>d</sup>, Ulf De Faire<sup>d</sup>,  
Nancy L. Pedersen<sup>j</sup>, Claes-Göran Östenson<sup>k</sup>, Laura Fratiglioni<sup>l</sup>, Mette Sørensen<sup>a</sup>,  
Kirsten T. Eriksen<sup>a</sup>, Anne Tjønneland<sup>a</sup>, Petra H. Peeters<sup>m,n</sup>, Bas Bueno-de-Mesquita<sup>n,o,p</sup>,  
Roel Vermeulen<sup>n,q,r</sup>, Marloes Eeftens<sup>q,s,t</sup>, Michelle Plusquin<sup>n</sup>, Timothy J. Key<sup>u</sup>, Andrea Jaensch<sup>d</sup>,  
Gabriele Nagel<sup>d,v</sup>, Hans Concini<sup>v</sup>, Meng Wang<sup>w</sup>, Ming-Yi Tsai<sup>s,t,w</sup>, Sara Grioni<sup>x</sup>,  
Alessandro Marcon<sup>y</sup>, Vittorio Krogh<sup>x</sup>, Fulvio Ricceri<sup>e,z</sup>, Carlotta Sacerdote<sup>e</sup>, Andrea Ranzi<sup>aa</sup>,  
Giulia Cesaroni<sup>c</sup>, Francesco Forastiere<sup>c</sup>, Ibon Tamayo<sup>bb,cc,dd</sup>, Pilar Amiano<sup>ee,ff</sup>,  
Miren Dorronsoro<sup>ee,ff</sup>, Leslie T. Stayner<sup>gg</sup>, Manolis Kogevinas<sup>bb,cc</sup>, Mark J. Nieuwenhuijsen<sup>bb,cc</sup>,  
Ranjeet Sokhi<sup>hh</sup>, Kees de Hoogh<sup>s,t</sup>, Rob Beelen<sup>q,ii</sup>, Paolo Vineis<sup>n,ij</sup>, Bert Brunekreef<sup>q,r</sup>,  
Gerard Hoek<sup>q</sup>, Ole Raaschou-Nielsen<sup>a,kk</sup>

<sup>a</sup> The Danish Cancer Society Research Center, Copenhagen, Denmark; <sup>b</sup> Centre for Epidemiology and Screening, Department of Public Health, University of Copenhagen, Copenhagen, Denmark; <sup>c</sup> Department of Epidemiology, Lazio Regional Health Service, Rome, Italy; <sup>d</sup> Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden; <sup>e</sup> Institute of Epidemiology and Medical Biometry, Ulm University, Ulm, Germany; <sup>f</sup> Unit of Cancer Epidemiology, Città della Salute e della Scienza University Hospital and Center for Cancer Prevention, Turin, Italy; <sup>g</sup> Occupational and Environmental Medicine, Department of Public Health and Clinical Medicine, Umea University, Umea, Sweden; <sup>h</sup> Norwegian Institute of Public Health, Oslo, Norway; <sup>i</sup> Department of Landscape Architecture and Spatial Planning, Norwegian University of Life Sciences, Ås, Norway; <sup>j</sup> Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Stockholm, Sweden; <sup>k</sup> Department of Molecular Medicine and Surgery, Karolinska Institute, Stockholm, Sweden; <sup>l</sup> Aging Research Center, Department of Neurobiology Care Science and Society, Karolinska Institute, Stockholm, Sweden; <sup>m</sup> Department of Epidemiology, Julius Center for Health Sciences and Primary Care, University Medical Center, Utrecht, The Netherlands; <sup>n</sup> MRC-PHE Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College, London, UK; <sup>o</sup> Department for Determinants of Chronic Diseases, National Institute for Public Health and the Environment, Bilthoven, The Netherlands; <sup>p</sup> Department of Social & Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; <sup>q</sup> Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands; <sup>r</sup> Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands; <sup>s</sup> Swiss Tropical and Public Health Institute, Basel, Switzerland; <sup>t</sup> University of Basel, Basel, Switzerland; <sup>u</sup> Cancer Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK; <sup>v</sup> Agency for Preventive and Social Medicine, Bregenz, Austria; <sup>w</sup> Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA, USA; <sup>x</sup> Epidemiology and Prevention Unit, Department of Preventive and Predictive Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; <sup>y</sup> Unit of Epidemiology & Medical Statistics, Department of Diagnostics and Public Health, University of Verona, Verona, Italy; <sup>z</sup> Unit of Epidemiology, Regional Health Service, Grugliasco, Italy; <sup>aa</sup> Environmental Health Reference Centre, Regional Agency for Environmental Prevention of Emilia-Romagna, Modena, Italy; <sup>bb</sup> Institute de Salut Global Barcelona, Barcelona, Spain; <sup>cc</sup> CIBER Epidemiología y Salud Pública, Madrid, Spain; <sup>dd</sup> Universitat Pompeu Fabra, Barcelona, Spain; <sup>ee</sup> Public Health Department of Gipuzkoa, BioDonostia Research Institute, San Sebastian, Spain; <sup>ff</sup> Consortium for Biomedical Research in Epidemiology and Public Health, Madrid, Spain; <sup>gg</sup> Division of Epidemiology and Biostatistics, School of Public Health, University of Illinois at Chicago, Chicago, IL, USA; <sup>hh</sup> Centre for Atmospheric and Instrumentation Research, University of Hertfordshire, Hatfield, UK; <sup>ii</sup> National Institute for Public Health (RIVM), Bilthoven, The Netherlands; <sup>jj</sup> Molecular and Epidemiology Unit, Human Genetics Foundation, Turin, Italy; <sup>kk</sup> Department of Environmental Science, Aarhus University, Roskilde, Denmark

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## Abstract

**Background:** Ambient air pollution contains low concentrations of carcinogens implicated in the etiology of urinary bladder cancer (BC). Little is known about whether exposure to air pollution influences BC in the general population.

**Objective:** To evaluate the association between long-term exposure to ambient air pollution and BC incidence.

**Design, setting, and participants:** We obtained data from 15 population-based cohorts enrolled between 1985 and 2005 in eight European countries ( $N = 303\,431$ ; mean follow-up 14.1 yr). We estimated exposure to nitrogen oxides ( $\text{NO}_2$  and  $\text{NO}_x$ ), particulate matter (PM) with diameter  $<10\ \mu\text{m}$  ( $\text{PM}_{10}$ ),  $<2.5\ \mu\text{m}$  ( $\text{PM}_{2.5}$ ), between 2.5 and  $10\ \mu\text{m}$  ( $\text{PM}_{2.5-10}$ ),  $\text{PM}_{2.5}$  absorbance (soot), elemental constituents of PM, organic carbon, and traffic density at baseline home addresses using standardized land-use regression models from the European Study of Cohorts for Air Pollution Effects project.

**Outcome measurements and statistical analysis:** We used Cox proportional-hazards models with adjustment for potential confounders for cohort-specific analyses and meta-analyses to estimate summary hazard ratios (HRs) for BC incidence.

**Results and limitations:** During follow-up, 943 incident BC cases were diagnosed. In the meta-analysis, none of the exposures were associated with BC risk. The summary HRs associated with a  $10\text{-}\mu\text{g}/\text{m}^3$  increase in  $\text{NO}_2$  and  $5\text{-}\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$  were 0.98 (95% confidence interval [CI] 0.89–1.08) and 0.86 (95% CI 0.63–1.18), respectively. Limitations include the lack of information about lifetime exposure.

**Conclusions:** There was no evidence of an association between exposure to outdoor air pollution levels at place of residence and risk of BC.

**Patient summary:** We assessed the link between outdoor air pollution at place of residence and bladder cancer using the largest study population to date and extensive assessment of exposure and comprehensive data on personal risk factors such as smoking. We found no association between the levels of outdoor air pollution at place of residence and bladder cancer risk.

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\* Corresponding author. Centre for Epidemiology and Screening, Department of Public Health, University of Copenhagen, Øster Farimagsgade 5, 1014 København K, Denmark.  
Tel. +45 60155545; Fax: +45 35327383.  
E-mail address: [mp@sund.ku.dk](mailto:mp@sund.ku.dk) (M. Pedersen).

## 1. Introduction

Urinary bladder cancer (BC) is the ninth most common cancer worldwide [1]. Smoking is the primary risk factor for BC, with relative risks of three for current smokers and two for former smokers compared to individuals who never smoked [2]. Findings from the most recent studies suggest that the relative risk for current smokers has increased to four or five times the risk for nonsmokers [3]. The relative risk for BC increases with smoking duration and intensity [4]. BC occurs mainly in older people, is more frequent in men, and exhibits large geographical variation [5].

Ambient air pollution includes a mix of carcinogens such as polycyclic aromatic hydrocarbons (PAHs), volatile organic compounds, transition metals, and diesel engine exhaust [6,7]. Ambient air pollution and particulate matter (PM) in ambient air have recently been classified as carcinogenic to humans [6]. This classification was largely based on higher risk of lung cancer [8–10]. However, there is suggestive evidence of an association between ambient air pollution and BC in humans [6,10].

Higher BC risk has been reported in some studies on taxi, bus, and/or truck drivers exposed to high levels of urban air pollution [6], including PAHs [11] and diesel engine exhaust [7], but no risk elevation was found for miners with high diesel exposure [12]. Some of these studies were

incidence-based, while others were based on mortality, which may also have contributed to the heterogeneity observed for results. A few studies have investigated a possible association between exposure to ambient air pollution and BC in the general population, and provided mixed results [13–17]. Limitations related to design, poor exposure assessment, and lack of information on potential confounding complicate interpretation of these previous studies.

Our aim was to examine the associations between exposure to ambient air pollution at the place of residence and BC incidence in a large European study population with fine-scale exposure assessment and extensive control for potential confounders such as smoking. We used the same study population, exposure assessment, and data analysis methods as in our previous study documenting significant associations between air pollution and lung cancer [9].

## 2. Materials and methods

### 2.1. Study population

The European Study of Cohorts for Air Pollution Effects (ESCAPE) project included 36 European areas where air pollution measurements were performed, exposure models were developed, and cohort studies located [9,18]. The present study included 15 population-based prospective

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